January 11, 2000

Alcon RESEARCH, LTD.

FEDERAL EXPRESS # **8157 3514 1262**
Dockets Management Branch (HFA-305)
Division of Management Systems and Policy
Office of Human Resources/Management Services
Food and Drug Administration
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RE: [Docket No. 99D-4054] Draft Guidance for Industry on Intraocular Lenses: Comments.

Dear Sir/Madam:

As described in Federal Register: October 14, 1999 (Volume 64, Number 198 / Notices / Page 55735 – 55736) Alcon Research, LTD. is taking this opportunity to submit comments for your consideration.

Page 5 - C. Abbreviations: *Add* FDIS – final draft international standard *since this abbreviation is used throughout this guidance document.*

Page 7 - C. Biocompatibility Tests (2): *Neither Genotoxicity nor the prescribed two extractants method is part of ISO/FDIS 11979-5 Annex D?*

Page 7 - C. Biocompatibility Tests (3): Maximization *Sensitization Test – Annex E of ISO/FDIS 11979-5 is "Selected Definitions" and does not outline or prescribe the two extractants process?*

Page 7 - C. Biocompatibility Tests (4): *Non-Ocular Animal Implantation Test – there is no Annex F in ISO/FDIS 11979-5?*

Page 7 - C. Biocompatibility Tests (5): *Ocular Implantation Test – there is no Annex F in ISO/FDIS 11979-5?*

Page 32 – VIII Labeling: *Adding an asterisk after the power constants denoting the basis of the constant (i.e. clinical or theoretical) and the month and year that it was established may not add value for the proper end-use of the device. It may be more appropriate to add alternative language in the package insert:*

"The suggested [A-Constant, Anterior Chamber Depth (ACD), or Effective Lens Position (ELP)] parameter values listed in the calculation table have been calculated using clinical data from the (model) lens." (Alternatively the sentence could read – calculated using theoretical analysis of the optical position of the lens inside the eye.). The values are starting points for implant power calculations. It is recommended that you develop you own A-Constant and..

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Page 32 continued...
..ACD/ELP values based on your experience with particular lens models, surgical techniques, measuring equipment, and postoperative results."

Page 34 – VIII Labeling: *Adding mechanical testing data to anterior chamber IOL insert labeling would not provide additional end-use information. This would most likely become a source of information for competitive lens analysis without any real benefit for the end-user. Propose deleting this section from the guidance document.*

Page 36 – IX Modifications (Level A 4.): *There is a requirement for the measurement of forces in the z-axis, however, there is no test method or criteria described. A proposed test method and criteria is provided as attachment #1 of this document.*

Pages 44 & 45– E Technology or Performance Changes:
- (2.a) *Delete hydrolytic stability. It would be highly unlikely to affect hydrolytic stability with changes to the IOL cleaning process.*

- *(2.c) Delete hydrolytic stability. It would be highly unlikely to affect hydrolytic stability with changes to the haptic staking process.*

- *(2.d) Delete hydrolytic stability. It would be highly unlikely to affect hydrolytic stability with changes to the annealing or a secondary manufacturing process. Also, add the word Curing to the category of changes (i.e. Annealing, Curing, or other secondary manufacturing processes).*

- *(2.e) Delete hydrolytic stability. It would be highly unlikely to affect hydrolytic stability with changes to the blocking or molding processes.*

- *(2.g) Delete hydrolytic stability. It would be highly unlikely to affect hydrolytic stability with changes to the tumbling process.*

Page 49 – E Labeling Changes: *Add a section to accommodate and recognize multi-lingual labeling in accordance with 21 CFR 801 as "No Prior Approval." Multi-lingual labeling has become standard industry practice since the implementation of the European Council Directive 93/42/EEC.*

Page 55 – ANNEX C (Informative) Sample Package Insert: *Remove the "prescription device statement" from the insert. It is more appropriate for this statement to be on the box label in accordance with 21 CFR 801.109. By the time the insert is accessed the device has been acquired and in use.*

Page 63 – ANNEX D (Informative) Format for Reporting Lens Modifications:
Sagitta is diopter dependent therefore it is not practical to list the value for each..

Page 63 continued...
..half diopter on the engineering drawing. Perhaps listing the range for available diopters would be more appropriate.

Alcon Research, LTD. appreciates the opportunity to provide input into the development of this guidance document. The final document will provide an excellent base of knowledge for Intraocular Lens Manufacturers and Distributors.

Sincerely,

John O'Riordan, Ph.D.
Associate Director
Surgical IOL / R&D

Timothy S. Adkins
Manager, Regulatory Affairs

PC: Rebecca Walker
Mary Pencis

Attachment #1

Z-Axis Force

Z-Axis force should be measured and reported at the same diameters that were used for the measurement of compression force.

Principle

Z-Axis force is measured with the IOL confined to a prescribed diameter.

Apparatus

Cylindrical well, with an inner diameter within ± 0.04 mm of that prescribed, with a base for loop location, and produced from a low friction material to minimize loop rotational constraint. Alternatively, two anvils with faces having a radius within ± 0.02 mm of that prescribed and produced from a low friction material to minimize loop rotational constraint.

Device capable of measuring force with a precision of ± 0.01 mN.

Device capable of measuring displacement with a precision of ± 0.01 mm.

Procedure

Test should be performed with the IOL in the horizontal plane and the lens at *in-situ* conditions with a temperature tolerance of ± 2^{0} C.

Place the IOL in the well and center the IOL manually as well as it can be done visually without exerting excessive force. Alternately, place the IOL between the anvils and close the anvils to the prescribed diameter.

As the optic is displaced anteriorly, record displacement and force.

Displace the optic until the most posterior point of the optic is 1 ± 0.05 mm from the anterior plane of the haptics.

Expression of Results

The test report will contain at least the following:

a) Test diameter;
b) Identification of the test sample;
c) Number of IOLs tested;
d) Arithmetic mean and standard deviation of test readings; and
e) Date of the test

Data Analysis

For a modified model to be considered a Level A modification of a parent model (or parent models), the following is required:

- No indication of haptic instability during the test.
- Some part of the z-axis force range of the modified model should overlap the range established by the parent or parents.

The z-axis force ranges for the modified model and the parent(s) are calculated using the following procedure:

- Determine the z-axis force range of the modified model.
  - If the standard deviation (σ) of the modified model is less than or equal to 20% of the mean, the z-axis force range of the modified model is equal to the mean $\pm$ (1)*σ.
  - If the standard deviation of the modified model is greater than 20% of the mean, the z-axis force range of the modified model is equal to the mean $\pm$ (0.2)* mean.
- Determine the z-axis force range of the parent(s).
  - If the standard deviation of the parent(s) is less than or equal to 20% of the mean, the z-axis fore range of the parent(s) is equal to the mean $\pm$ (3)*σ.
  - If the standard deviation of the parent(s) is greater than 20% of the mean, the z-axis force range of the parent(s) is equal to the mean $\pm$ (3)*(0.2)*mean.

End of Document.
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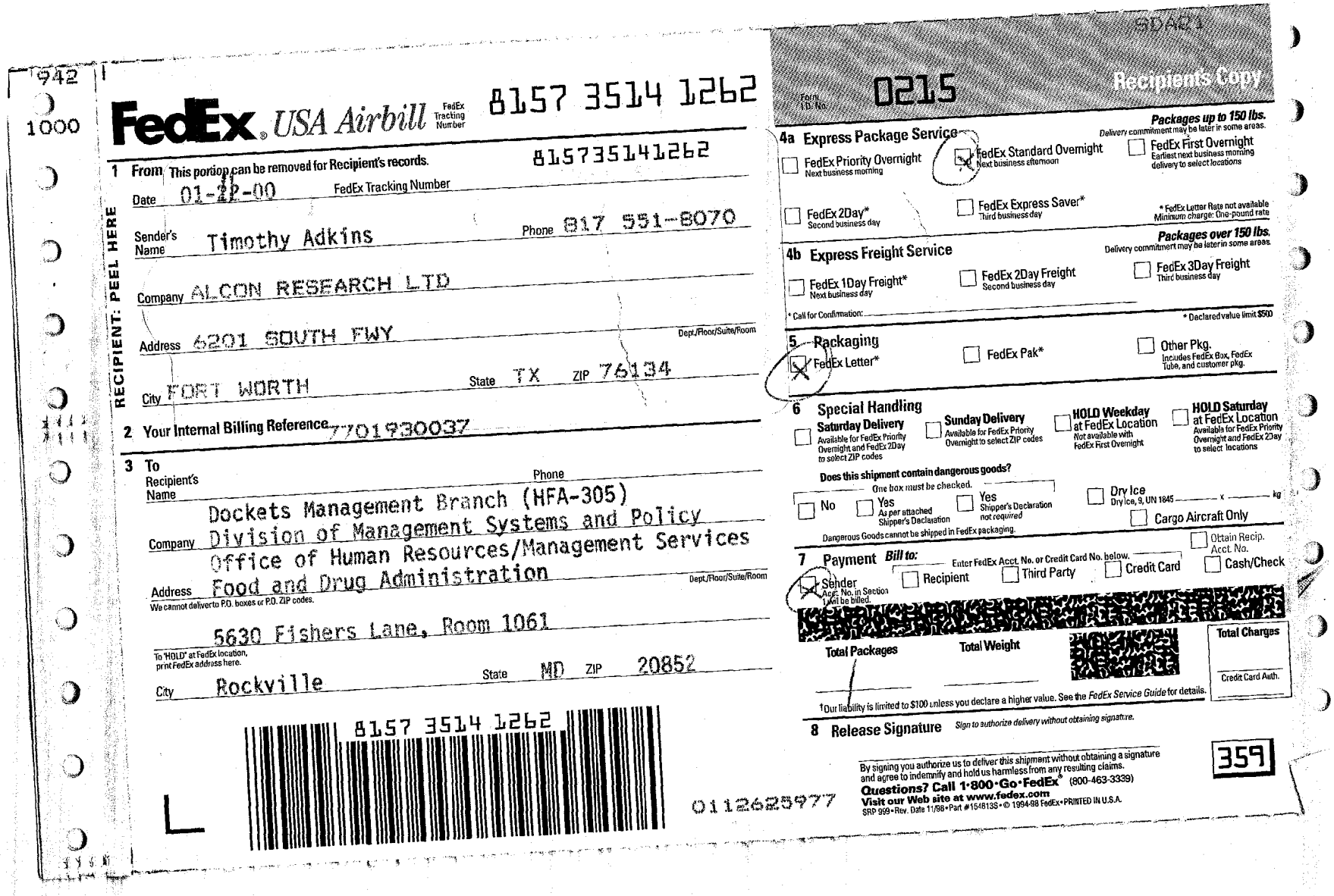

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